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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/963,340	09/24/2001	Mark A. Conkling	5051.338CT	1188

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EXAMINER	
KALLIS, RUSSELL	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 04/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/963,340	CONKLING ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-93* is/are pending in the application.

4a) Of the above claim(s) *14,15 and 63-93* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 16-62* is/are rejected.

7)☐ Claim(s) ____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 December 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, Claims 16-62 in Paper No. 10/01/2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-93 are pending. Claims 1-13 and 16-62 are examined. Claims 14-15 and 63-93 are withdrawn.

Priority

This application filed under former 37 CFR 1.62 lacks the necessary reference to the prior application. A statement reading "This is a continuation of Application No. 09/021,286 filed 02/10/1998 now U.S. Patent 6,586,661." should be entered following the title of the invention or as the first sentence of the specification. Also, the current status of the parent nonprovisional application(s) should be included.

Claim Objections

Claims 1, 7-9, 12, 16, 22-23, 26, 31-38, 40-41, 46, 48 and 57-58 are objected to because of the following informalities:

Claim 1, in line 1, "DNA molecule" and in lines 4, 5 and 7, "DNA sequences"; switching from singular to plural is inconsistent.

Claims 7, 8, 22, 23, 40 and 41 the use of the word "tissue" is redundant.

Claim 9, the inclusion of a plasmid is confusing.

Claim 12, for clarity "A plant cell containing" should read "A plant cell transformed with".

Claim 16, lines 9-10, "transformed cells" and "said plant cell"; switching from singular to plural is inconsistent.

Claim 26 improperly claims dependence to a later recited claim, Claim 32.

In Claim 31 and throughout the claims, species *Nicotiana* is incorrect. *Nicotiana* is a genus.

Claims 31-38, the claims are improperly dependent. Claim 31 is not a method claim.

Claim 31, line 6, after "DNA" insert --sequence--.

In Claim 46, line 6, after "phosphoribosyl" insert --transferase--.

In Claim 48, line 5, after "DNA" insert --sequence--.

In Claim 57 line 6, after "said" insert --exogenous--.

In Claim 58, line 2 after "sequence" insert --is--.

Appropriate correction is required.

Drawings

The drawings are objected to because they contain copying artifacts. Corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Information Disclosure Statement

The information disclosure statement filed 09/24/2001 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. The Examiner requests that Appplicant send a copy of all non-US Patent IDS references for IDS submitted 9/24/2001.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 and 16-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims an isolated DNA of SEQ ID NO: 1 encoding a quinolate phosphoribosyl transferase enzyme of SEQ ID NO: 2, isolated DNA sequences that encode SEQ ID NO: 2 and DNA sequences that hybridize therewith; an isolated DNA encoding a plant quinolate phosphoribosyl transferase and plants comprising DNA segments thereof; a method of making a transgenic plant cell having reduced QRPTase expression or a method of reducing expression of a QPRTase in a transformed plant using any portion of a sequence encoding a

QPRTase mRNA in sense or antisense orientation; or using at least any 15, any 200, or any number of 3' or 5' untranslated nucleotides complementary to a QPRTase mRNA; and a method of producing a tobacco plant having reduced levels of nicotine therewith, and transformed plants and seeds thereof.

Applicant describes SEQ ID NO: 1 encoding SEQ ID NO: 2

Applicant does not describe any other DNA sequence or portions thereof encoding any other quinolate phosphoribosyl transferase mRNA other than SEQ ID NO: 1 encoding SEQ ID NO: 2.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicants fail to describe a representative number of polynucleotide sequences falling within the scope of the claimed genus of polynucleotides encoding an isolated DNA of SEQ ID NO: 1 encoding a quinolate phosphoribosyl transferase enzyme of SEQ ID NO: 2; isolated DNA sequences that encode SEQ ID NO: 2 and DNA sequences that hybridize therewith; an isolated DNA encoding a plant quinolate phosphoribosyl transferase and plants comprising DNA segments thereof; a method of making a transgenic plant cell having reduced QRPTase expression using any portion of a sequence encoding a QPRTase mRNA in sense or antisense orientation; or using at least any 15, any 200, any number of 3' or 5'

untranslated nucleotides complemntary to a QPRTase mRNA; a method of reducing QPRTase expression in a transformed plant using an exogenous DNA sequence or portions thereof complementary to a quinolate phosphoribosyl transferase mRNA; methods of transforming a plant and reducing QPRTase and nicotine levels in a plant therewith.

Applicants only describe a single cDNA (SEQ ID NO: 1) and the amino acid sequence of the QPRTase enzyme it encodes (SEQ ID NO: 2).

Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for CCA1 protein activity, it remains unclear what features identify a QPRTase encoding polynucleotide and the accompanying untranslated regions. Since the genus of QPRTase encoding polynucleotides or segments or portions, or untranslated regions thereof has not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

Sequences that encode an isolated DNA encoding a quinolate phosphoribosyl transferase enzyme; an isolated DNA of SEQ ID NO: 1 encoding a quinolate phosphoribosyl transferase enzyme of SEQ ID NO: 2; isolated DNA sequences that encode SEQ ID NO: 2 and DNA sequences that hybridize therewith; portions of a DNA sequence encoding a quinolate phosphoribosyl transferase mRNA; a DNA sequence having at least 15 nucleotides complementary to a DNA sequence encoding a quinolate phosphoribosyl transferase mRNA; a DNA sequence having at least 200 nucleotides complementary to a DNA sequence encoding a quinolate phosphoribosyl transferase mRNA; and untranslated 3' and 5' regions of any DNA

encoding a quinolate phosphoribosyl transferase mRNA encompass naturally occurring allelic variants, mutants of QPRTase encoding polnucleotides, as well as sequences encoding proteins having no known QPRTase activity, of which Applicant is not in possession. Accordingly, the specification fails to provide an adequate written description to support the genus of polynucleotides encompassed by the hybridization language. (See Written Description guidelines published in Federal Register/Vol. 66, No.4/Friday, January 5, 2001/Notices: p.1099-1111).

Claims 1-13 and 16-62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO: 1 encoding SEQ ID NO: 2, tobacco plants transformed with an antisense copy of SEQ ID NO: 1, a method of reducing QPRTase expression in transformed tobacco cells and tobacco plants, and a method of reducing nicotine levels in tobacco plants transformed with an antisense DNA of SEQ ID NO: 1, does not reasonably provide enablement for using any DNA sequence encoding any QPRTase or any portion or segment thereof, or a method of reducing QPRTase expression or nicotine levels in any plant other than a method of reducing QPRTase expression in a tobacco plant transformed with antisense DNA of SEQ ID NO: 1 and transformed tobacco plants therewith. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of

experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Applicant broadly claims an isolated DNA of SEQ ID NO: 1 encoding a quinolate phosphoribosyl transferase enzyme of SEQ ID NO: 2, isolated DNA sequences that encode SEQ ID NO: 2 and DNA sequences that hybridize therewith; an isolated DNA encoding a plant quinolate phosphoribosyl transferase and plants comprising DNA segments thereof; a method of making a transgenic plant cell having reduced QRPTase expression or a method of reducing expression of a QPRTase in a transformed plant using any portion of a sequence encoding a QPRTase mRNA in sense or antisense orientation; or using at least any 15, any 200, or any number of 3' or 5' untranslated nucleotides complementary to a QPRTase mRNA; and a method of producing a tobacco plant having reduced levels of nicotine therewith, and transformed plants and seeds thereof.

Applicant teaches SEQ ID NO: 1 encoding SEQ ID NO: 2 and the recovery of QPRTase activity in a *nadC* mutant of *E. coli* transformed with SEQ ID NO: 1 (Example 1, page 22 and Example 5, page 25); transformation of tobacco with antisense DNA of SEQ ID NO: 1, and a method of reducing nicotine levels in tobacco plants transformed with an antisense DNA of SEQ ID NO: 1.

Applicant does not teach any plant DNA sequence that encodes a QPRTase, other than SEQ ID NO: 1, or any plant, other than tobacco, transformed with a construct comprising SEQ ID NO: 1 that has reduced expression of the endogenous QPRTase and reduced levels of

nicotine. The specification fails to provide guidance for portions or segments of any QPRTase encoding DNA sequence, or which 5' and 3' untranslated regions thereof, that would enable the methods of the claims.

The state of the art for manipulation of plant metabolism/phenotype using transgenes is highly unpredictable in any particular plant species where the DNA sequences required to affect that aspect of metabolism are not taught and would require using known orthologous genes. Even a careful consideration of the likely reduction in sequence identity or homology of the transgene or portions of the transgene to the target gene in closely or distantly related species, uncharacterized with respect to the number of target gene isoforms or the specific degree of sequence identity between the transgene or parts of the transgene and the endogenously expressed DNA sequence, cannot reliably predict the biochemical properties or interactions of the transgene and endogenous gene product and hence the phenotype from expression of a particular transgene or transgene portion cannot be reliably predicted (Wu K. *et al.,* Plant Physiology, 1997, Vol. 114, pp. 1421-1431; page 1430 column 1, lines 11-27 and last paragraph lines 5-9). For example, antisense expression of a *gchs2* gene resulted in only partial reduction of *gchs3* and *gchs1* isoforms of the gene in transgenic *Gerbera hybrida* (Elomaa P. *et al.*, Molecular Breeding 1996, Vol. 2, pp. 41-50; on page 48, column 2 lines 4-10). Similarly, the co-suppression of gene expression is dependent upon a high degree or at least a recognizable degree of sequence identity or homology between transgene and target sequence (Waterhouse P. *et al.,* Trends in Plant Sciences, November 1999, Vol. 4, No. 11 pp. 452-457; page 453 column 1 lines 32-40).

Based upon Applicant's limited guidance one cannot predict which embodiments would be operable and thus undue trial and error experimentation would be required by one of skill in the art to isolate and test the multitude of non-exemplified DNA sequences for QPRTase activity and transform and screen a myriad of non-exemplified transformed plants from any species for reduced QPRTase expression and nicotine content encompassed by the claims.

Given the unpredictability in the art as to which QPRTase encoding DNA sequences or portions or segments thereof when transformed into any plant would reduce expression of an endogenous QPRTase and reduce nicotine levels; the breadth of the claims encompassing any plant transformed with any polynucleotide encoding a QPRTase having reduced QPRTase expression or reduced levels of nicotine; the lack of guidance in the examples of the specification or in the prior art as to which nucleotide sequences, or portions or segments thereof, would reduce QPRTase expression levels or reduce levels of nicotine in a transformed; and the undue trial and error experimentation required to practice the claimed invention, the invention is not enabled for the scope set forth in the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-13, 16-25 and 27-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claim 1, parts (b) and (c) "DNA sequences" lacks antecedence.

In Claim 2, "which construct" and "a DNA segment" lack antecedence. "Which construct" should refer back to the cassette.

In Claim 3, "which construct", "a DNA segment" and "said DNA segment" lack antecedence. "Which construct" should refer back to the cassette.

In Claim 13, there is no antecedence for "plant cells".

In Claim 16, line 6, "portion" is a relative term. It is not clear whether the portion is the entire portion or some other part.

In Claim 17, line 1, "portion" is a relative term. It is not clear whether the portion is the entire portion or some other part.

In Claim 18, line 1, "portion" is a relative term. It is not clear whether the portion is the entire portion or some other part.

Claims 27-30, line2, there is no antecedence for "sequence" and "a quinolate phosphoribosyl transferase messenger RNA".

In Claim 31, line 5, there is no antecedence for "said plant cell".

In Claims 32-33, "wherein said segment of DNA comprising" lacks antecedence. The claim should read --wherein said DNA comprising--.

In Claim 45, there is no antecedence for "A crop comprising a plurality of plants" or "plurality of plants" in Claim 31.

In Claim 46, line 5, "said complementary strand" lacks antecedence. It should be changed to --said exogenous DNA--.

In Claim 52, line 2, "sequence" lacks antecedence.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 44 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claimed inventions encompass untransformed plants and seeds, which are a product of nature and not one of the five classes of patentable subject matter. Claim 44 is drawn to parts such as seeds and progeny of the transformed plant. Due to Mendelian inheritance of genes, a single gene introduced into a parent plant would only be transferred at most to half the male gametes and half the female gametes. This translates into only two thirds of the progeny having at least a single copy of the transgene and one quarter of the progeny would not carry a copy of the transgene. Since the claim encompasses progeny that lack the transgene, the claim encompasses plants and seeds that are indistinguishable from plants and seeds that would occur in nature. See *American Wood v. Fiber Distintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Hughes K. *et al.*, Journal of Bacteriology; January 1993, Vol. 175, No. 2; pages 479-486.

The cited reference teaches a *nadC* cDNA sequence encoding a bacterial QPRTase in Figure 3 on page 483 and a T7 promoter operable in a plant cell operably associated with the *nadC* cDNA sequence on page 483 column 2. Thus, the reference teaches all the limitations of Claims 1-2.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-13, 16-26, 31, 43-46 and 57 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-32 of U.S. Patent No. 6,586,661 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both directed to an isolated DNA comprising the DNA sequence of SEQ ID NO: 1 which encodes a quinolate phosphoribosyl transferase enzyme, a DNA construct thereof, transgenic plants and seeds transformed therewith, methods of transforming plants and plant cells with SEQ ID NO: 1 and of reducing expression of quinolate phosphoribosyl transferase expression in a plant cell or plant transformed with SEQ ID NO: 1 in

sense or antisense orientation, and a method of reducing nicotine levels in tobacco transformed with an antisense construct comprising SEQ ID NO: 1.

All claims are rejected.

Claims 3-13 and 16-62 are deemed free of the prior art given the failure of the prior art to teach or suggest DNA sequences encoding a QPRTase and methods of making plant cells and plants transformed therewith wherein the levels of QPRTase or nicotine are reduced.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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March 25, 2004

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